PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	)	
	)	Group Art Unit :
Briggs and Tatum	)	
	)	Examiner:
Serial No. TBA	)	
DIV of 09/245,331	)	
	)	Atty. Docket No. 000295.00014
Filed: even herewith	)	

For: ***LKTA* Deletion Mutant of *P. haemolytica***

EXPRESS MAIL CERTIFICATE

PRELIMINARY AMENDMENT

Assistant Director for Patents
Washington, D.C. 20231

Sir:

Before examining the divisional application referenced above, please enter the following amendments. Appendix 1 is a copy of the amended paragraphs, with markings to show changes made.

We believe no fee is due in connection with this amendment. If a fee is due, please charge Deposit Account No. 19-0733.

IN THE SPECIFICATION

(1) On page 1, after the title, please delete the paragraph at lines 3-5 and substitute the following paragraph:

This application is a division of Serial No. 09/245,331 filed February 5, 1999, which is a

continuation in part of Serial No. 09/160,340 filed September 25, 1998, which claims the benefit of co-pending provisional application Serial No. 60/060,060, filed September 25, 1997. Each of these applications is incorporated by reference herein.

(2) On page 2, delete the paragraph at lines 26-29 and substitute the following paragraph:

Still another embodiment of the invention provides a temperature sensitive plasmid. The plasmid replicates at 30 °C but not at 40 °C in *P. haemolytica*. Moreover, it is of the same incompatibility group as the plasmid which has been deposited at the ATCC with Accession No. 98895.

(3) On page 4, delete the paragraph at lines 19-23 and substitute the following paragraph:

Also provided by the present invention is a temperature sensitive plasmid which replicates at 30 °C but not at 40 °C in *P. haemolytica*. Preferably the plasmid is of the same incompatibility group as pD80, *i.e.*, it shares the same origin of replication. One such plasmid has been deposited at the ATCC with Accession No. 98895.

IN THE CLAIMS

Please delete claims 1-34 and substitute the following new claims.

35. (new) A method of inducing immunity to pneumonic pasteurellosis in ruminants, comprising the step of:

administering to a ruminant a *P. haemolytica* bacterium which (a) expresses no biologically active leukotoxin, (b) expresses a form of leukotoxin molecule which induces antibodies which neutralize biologically active leukotoxin, and (c) contains no non-*P.*

haemolytica DNA, whereby immunity is induced.

36. (new) The method of claim 35 wherein the step of administering is via the oral route.

37. (new) The method of claim 36 wherein the bacterium is top-dressed on the feed of the ruminant.

38. (new) The method of claim 35 wherein the step of administering comprises injecting the bacterium subcutaneously.

39. (new) The method of claim 35 wherein the step of administering comprises injecting the bacterium intradermally.

40. (new) The method of claim 35 wherein the step of administering comprises injecting the bacterium intramuscularly.

41. (new) The method of claim 35 wherein the step of administering is via the nose.

42. (new) The method of claim 35 wherein the bacterium is live.

43. (new) The method of claim 35 wherein the bacterium is lyophilized.

44. (new) The method of claim 35 wherein the bacterium is lyophilized and reconstituted.

45. (new) The method of claim 35 wherein the bacterium is killed.

46. (new) A feed for ruminants which comprises a *P. haemolytica* bacterium which (a) expresses no biologically active leukotoxin, (b) expresses a form of leukotoxin molecule which induces antibodies which neutralize biologically active leukotoxin, and (c) contains no non-*P. haemolytica* DNA, whereby immunity is induced.

47. (new) The feed of claim 46 wherein the bacterium is live.

48. (new) The feed of claim 46 wherein the bacterium is lyophilized.

49. (new) The feed of claim 46 wherein the bacterium is lyophilized and reconstituted.

50. (new) The feed of claim 46 wherein the bacterium is killed.

51. (new) A vaccine for reducing morbidity in ruminants, comprising a *P. haemolytica* bacterium which (a) expresses no biologically active leukotoxin, (b) expresses a form of leukotoxin molecule which induces antibodies which neutralize biologically active leukotoxin, and (c) contains no non-*P. haemolytica* DNA.

52. (new) The vaccine of claim 51 wherein the bacterium is live.

53. (new) The vaccine of claim 51 wherein the bacterium is lyophilized.

54. (new) The vaccine of claim 51 wherein the bacterium is lyophilized and reconstituted.

55. (new) The vaccine of claim 51 wherein the bacterium is killed.

56. (new) A temperature sensitive plasmid which replicates at 30 °C but not at 40 °C in P. haemolytica and which has an origin of replication of the same incompatibility group as the plasmid which has been deposited at the ATCC with Accession No. 98895.

57. (new) The temperature sensitive plasmid of claim 48 which is the plasmid which has been deposited at the ATCC with Accession No. 98895.

58. (new) A method of inducing immunity to pneumonic pasteurellosis in ruminants, comprising the step of:

administering to a ruminant a *P. haemolytica* leukotoxin protein which (a) is biologically inactive, (b) induces antibodies which neutralize biologically active leukotoxin, and (c) contains no foreign amino acid sequences, whereby immunity is induced.

59. (new) The method of claim 58 wherein the step of administering is via the oral route.

60. (new) The method of claim 58 wherein the leukotoxin protein is top-dressed on the

feed of the ruminant.

61. (new) The method of claim 58 wherein the step of administering comprises injecting the leukotoxin protein subcutaneously.

62. (new) The method of claim 58 wherein the step of administering comprises injecting the leukotoxin protein intradermally.

63. (new) The method of claim 58 wherein the step of administering comprises injecting the leukotoxin protein intramuscularly.

64. (new) The method of claim 58 wherein the step of administering is via the nose.

65. (new) A vaccine for reducing morbidity in ruminants, comprising a *P. haemolytica* leukotoxin protein which (a) is biologically inactive, (b) induces antibodies which neutralize biologically active leukotoxin, and (c) contains no foreign amino acid sequences, whereby immunity is induced.

Remarks

The specification is amended to insert the priority information and the ATCC accession number of the temperature-sensitive plasmid.

New claims 35-41, 46, 51, 5-57, and 58-65 are directed to the same subject matter claimed in canceled claims 9-15, 16, 17, 18-19, and 26-34, respectively. New claims 42-45, 47-50, ad 52-55 are supported at page 4, lines 14-15: "The bacteria in the vaccine formulation can be live, lyophilized, lyophilized and reconstituted, or killed."

No new matter is added.

Respectfully submitted,

Date: 1-25-02

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Appendix 1. Version of the amended paragraphs, with markings to show changes made.

Page 1, lines 3-5:

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Page 2, lines 26-29:

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Page 4, lines 19-23:

Also provided by the present invention is a temperature sensitive plasmid which replicates at 30 °C but not at 40 °C in *P. haemolytica*. Preferably the plasmid is of the same incompatibility group as pD80, *i.e.*, it shares the same origin of replication. One such plasmid has been deposited at the ATCC with Accession No. [_____] 98895.